MEG evaluation in temporal lobe epilepsy

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1 Introduction

Temporal lobe epilepsies represent the most frequent form of focal epilepsies [1]. The seizures are frequently difficult to control with antiepileptic medication and eventually 30-50% of patients have to be considered as medically refractory. Epilepsy surgery can be considered as a valuable treatment option for these patients rendering 70-90% of them seizure-free [2]. Thus, exact localization of both the epileptogenic zone and essential brain regions which can only be accomplished during a thorough presurgical work-up is crucial for a successful surgical treatment and the improvement of non-invasive methods is clinically warranted.

Magnetoencephalography (MEG) could improve the non-invasive evaluation of temporal lobe epilepsy patients for several reasons.

First, MEG provides a superior spatial resolution as compared to scalp-EEG because magnetic fields are far less distorted than electric fields by the resistive properties of the skull and scalp measured [3]. Second, the advent of whole-head MEG systems represented a major breakthrough because simultaneous recordings from the entire brain can be obtained which is critical for the assessment of spontaneous brain activity.

Thus, magnetic field generated by epileptic activity can be mapped in a single shot without repositioning the MEG probe inevitable with previous multichannel MEG systems [4].

While numerous MEG studies in human temporal lobe epilepsy have been published [5-11], only few studies systematically assessed the merit of MEG in clearly defined temporal lobe syndromes [12,13] and its impact as well as practicability in a clinical setting [14]. We therefore assessed the following questions concerning MEG in temporal lobe epilepsy:

1. What is the diagnostic yield of MEG in temporal lobe epilepsy? Are there differences in diagnostic yield for the various subgroups of temporal lobe epilepsy?
2. What is the role of MEG for the evaluation of specific temporal lobe epilepsy syndromes, i.e. mesial TLE, non-lesional TLE and lesional TLE?

2 Methods

2.1 Patients

We studied a total of 49 patients suffering from medically refractory temporal epilepsy who were evaluated in our epilepsy monitoring unit for possible epilepsy surgery. 26 patients suffered from mesial temporal lobe epilepsy (mesial TLE). 15 patients were diagnosed as non-lesional temporal lobe epilepsy (non-lesional TLE). Finally, in 8 patients structural lesions within the temporal lobes could be identified on MRI. As clinical seizure semiology, interictal spikes and ictal EEG changes proved that the lesions were responsible for the patients' seizures, these patients were classified as lesional temporal lobe epilepsy (lesional TLE).

All patients underwent an extensive presurgical work-up including intensive video-EEG-monitoring, high resolution MRI-scan, interictal SPECT, formal neuropsychological testing and an intracarotid sodium amytal test.

2.2 MEG recordings

MEG recordings were performed in all patients for a duration of 2-3 hours. MEG was performed with a 143 channel whole-head MEG (CTF Systems Inc., Port Coquitlam, B.C. Canada) in a large magnetically shielded room (Vacuumschmelze GmbH, Hanau, Germany). The MEG system consisted of an array of 143 first order axial gradiometers with 2 cm diameter and 5 cm baseline, uniformly distributed in a helmet-shaped liquid helium dewar. The average coil center separation was 3.2 cm covering the head down to an extent of 130 degrees from the vertex [15]. Scalp-EEG was recorded simultaneously from 23-26 gold-disk electrodes placed according the International 10-20 System with additional basal temporal electrodes. MEG signals were amplified, filtered (bandpass 1-70 Hz), analog-to-digital converted (sampling frequency = 250 Hz, 12 bits) and stored digitally for off-line data analysis.

We used spontaneous spikes for dipole analysis in order to avoid introducing artificial time delays by averaging variable spike populations. After visual inspection of the data and artifact rejection, we first calculated isofield maps using spherical spline interpolation. We then applied dipole modeling to calculate backwards unto the neuronal sources underlying the epileptic spike complex. We assumed a single equivalent current dipole as neural source and a spherical head model as volume conductor. The goal of the program was to find which combination of dipole location and orientation parameters most closely reproduced the data using a non-linear least squares minimization procedure.

In order to correlate source localizations with anatomical structures on MRI, head position with respect to the sensing gradiometers was monitored by tracking 3 small coils placed at anatomical landmarks of the head, i.e. the nasion, the right and left pre-auricular points, defining a head based coordinate system during the MEG recording session [15]. Subsequently, MRI scans were performed with lipid-filled capsules placed at these fiducial points.

3 Results

3.1 Diagnostic yield of MEG

During the MEG recordings interictal spikes could be recorded in 11 out of 26 patients with mesial TLE (= 42.3%), in 11 of 15 patients with non-lesional TLE (= 73.3%) and in 4 out of 8 patients with lesional TLE (= 50.0%; p=0.154). Although in most cases, interictal spikes could be identified both on scalp-EEG and MEG, in some instances spikes were visible on scalp-EEG but not on MEG, while the reverse, i.e. MEG spikes without EEG spikes occurred less often.

3.2 Mesial temporal lobe epilepsy

In patients with mesial TLE all spike dipoles could be localized to the temporal lobe with a clear preponderance of its medio-basal aspects. We observed two types of dipole orientations. In 6 patients interictal spikes could be modeled by so-called ‘anterior temporal vertical dipoles’ which were oriented vertically with their positive poles directed towards the vertex and their negative poles towards the basal temporal region resulting in a magnetic field emerging from the head at the anterior temporal and frontal recording positions and re-entering the head at the posterior temporal, temporo-parietal and temporo-occipital sensor positions (Fig. 1). In the other 5 patients so-called ‘anterior temporal horizontal dipoles’ were observed which were characterized by a horizontal orientation with their positive poles oriented posterior and their negative poles oriented anterior producing a magnetic field pattern emerging from the head at the inferior temporal sensor positions and re-entering the head at the superior temporal and central sensor locations (Fig. 2).

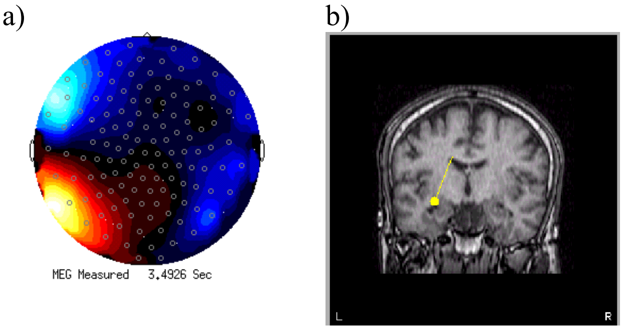

Figure 1: *Mesial temporal lobe epilepsy: anterior temporal vertical dipole: a) Isofield map and b) dipole localization projected unto MRI scan.*

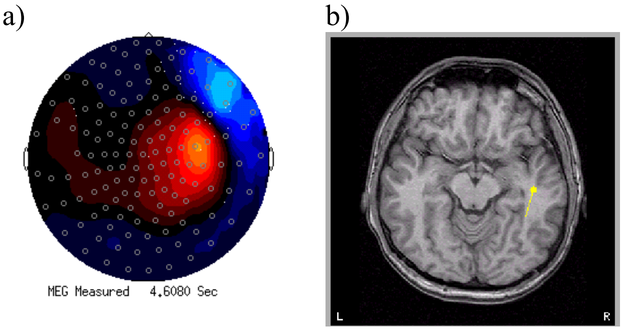

Figure 2: *Mesial temporal lobe epilepsy: anterior temporal horizontal dipole: a) Isofield map and b) dipole localization projected unto MRI scan*

3.3 Non-lesional temporal lobe epilepsy

Whereas in 5 patients dipole sources were localized to the anterior medial temporal lobe, in the other 6 patients dipole localizations were attributed to the posterior and lateral temporal lobe. Dipole orientation was vertical in all patients with the positive poles directed superior and the negative poles inferior generating a magnetic field pattern emerging from the head at the anterior temporal and frontal recording positions and re-entering the head at the posterior temporal, temporo-parietal and temporo-occipital region (Fig. 3). In 3 patients - one with a medial and two with lateral vertical dipoles - invasive recordings with chronically indwelling subdural grid electrodes were performed. Whereas the seizure onset zone was confined to the medial temporal lobe in the patient with medial MEG spikes, in the other two patients with lateral MEG spikes invasive seizure onset was more widespread involving both the lateral and medial temporal contacts.

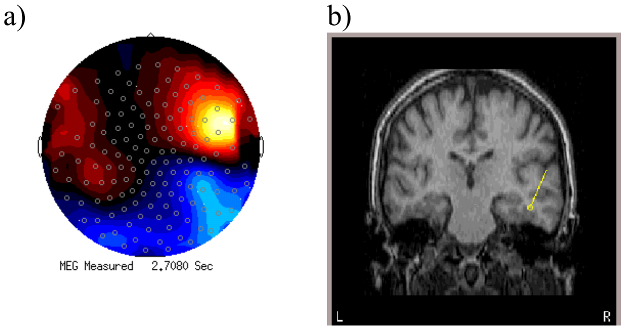

Figure 3: *Nonlesional temporal lobe epilepsy: posterior lateral temporal vertical dipole: a) Isofield map and b) dipole localization projected unto MRI scan*

3.4 Lesional temporal lobe epilepsy

In patients with lesional TLE, MEG spike dipoles could be localized within or in the immediate vicinity of the lesion. Dipole orientations were variable across patients. We also studied a patient who had undergone a prior lesionectomy of a pilocytic astrocytoma. After an initial seizure-free interval the patient continued to experience seizures. MEG localized the most active spiking zone to the lateral border of the resection (Fig. 4).

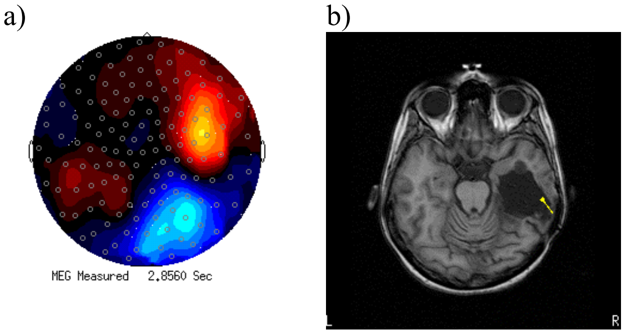

Figure 4: *Lesional temporal lobe epilepsy: anterior temporal horizontal dipole: a) Isofield map and b) dipole localization projected unto MRI scan.*

4 Discussion

4.1 Diagnostic yield of MEG

In our patients the diagnostic yield of MEG during a single 2-3 hour recording session was 53.1%. During intensive video-EEG monitoring on the contrary, spikes could be recorded in all patients.

Interictal spikes were recorded more often in patients with non-lesional TLE (73.3%) as compared to patients with mesial (42.3%) or lesional (50%) TLE although this difference did not reach statistical significance. Thus, MEG seems to be more sensitive to detect spikes in neocortical epilepsy which also was evident in a previous study where MEG spikes could be detected in 92% of patients with neocortical epilepsy, but only in 50% of patients with mesial TLE [14].

There were more EEG spikes without simultaneous MEG spikes than MEG spikes without EEG spikes which is in agreement with previous combined MEG and EEG studies [9,16]. This finding can be explained by the selective sensitivity of MEG for tangential sources, while radial sources do not produce a detectable MEG signal.

4.2 Interictal spikes in mesial temporal lobe epilepsy

In mesial temporal lobe epilepsy the dipolar sources underlying the interictal spike complex could be localized to the temporal lobe with a predominance of its medio-basal aspects in all patients. However, dipole localizations have to be interpreted with respect to the basic modeling assumptions underlying source modeling.

Based on orientation dipoles could be classified into two types, namely an anterior temporal vertical dipole and an anterior temporal horizontal dipole. Dipole orientations were useful to identify temporal lobe subcompartments involved in epileptic activity. Thus, our anterior temporal vertical dipole is compatible with epileptic activity in the medio-basal temporal lobe and corresponds closely to the type 1 dipoles defined by Ebersole and Wade [17,18] using spike voltage topography and single instantaneous dipole modeling on scalp-EEG.

The anterior horizontal dipole can be explained by epileptic activity of the temporal tip cortex as proposed by Ebersole [13].

We therefore believe that dipole orientations are more important than absolute dipole localizations for an appropriate delineation of the irritative zone from MEG recordings.

4.3 Non-lesional temporal lobe epilepsy

Non-lesional epilepsy poses a major challenge in presurgical epilepsy evaluation because these patients usually require invasive recordings to adequately define the seizure onset zone [1].

In our 11 patients with non-lesional TLE, MEG spike dipoles were localized either to the anterior medial (n=5) or to the posterior lateral temporal lobe (n=6). Dipole orientation was vertical in all cases. In the 3 patients in whom invasive recordings were performed the invasive EEG seizure onset agreed very well with the interictal MEG dipole localizations. Our results thus concur with the findings of Ebersole[13].

In conclusion, interictal MEG spike dipole modeling may become a useful non-invasive method to differentiate mesial from lateral temporal epileptogenic zones in patients with normal MRI scans.

4.4 Lesional temporal lobe epilepsy

In our patients with lesional TLE, MEG spike dipoles could be localized adjacent to the lesions visible on MRI scans. Numerous interictal MEG studies in patients with temporal lobe structural lesions have been reported [5,10,11,14]. MEG provided useful information for the placement of invasive electrodes and the planning of surgical strategy in these patients [18]. Furthermore, MEG may help to clarify the still poorly understood relationship of discrete lesions to the generation of seizures and more specifically whether lesionectomy alone or resection of the lesion plus the adjacent epileptogenic zone should be performed in these patients [19].

5 Conclusion

The introduction of whole-head MEG systems has lead to a major breakthrough of the MEG application in clinical epileptology. MEG is useful to identify subcompartments of the temporal lobe involved in epileptic activity. Dipole orientations are more important than absolute dipole localizations for an appropriate delineation of the irritative zone. Whether the two dipole types identified in mesial TLE are of prognostic significance for surgical outcome and whether their occurrence should influence the surgical strategy remains to be determined. In non-lesional TLE MEG may help to differentiate between mesial, lateral or diffuse seizure onset zones and thus could reduce the need of invasive procedures in these patients. In lesional TLE MEG can help to define the spatial relationship between the structural lesion and the irritative zone which is important for surgical planning. Especially patients with persistent seizures after lesionectomy or epilepsy surgery will benefit from MEG, because the magnetic fields are less distorted by skull and dura defects introduced by the prior operation. The sensitivity of MEG seems to be higher in lateral TLE as compared to mesial TLE which underlines its potentials for the investigation of non-lesional neocortical TLE. MEG therefore can be regarded as a useful, clinically relevant non-invasive method to better define the interictal irritative spike zone in patients with temporal lobe epilepsies.

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